

AMENDMENT TO THE SPECIFICATION

Applicants respectfully request amendment of the following paragraphs of the specification:

Please delete paragraph 1, before the Background of the Invention section, on page 1 of the application and replace it with the following paragraph:

This is a National Stage Application of International Application No. PCT/US2004/06043, filed May 21, 2004, and claims the benefit of priority of application No. 10/774,048, filed on February 04, 2004, now abandoned, which claims the benefit of U.S. provisional application No. 60/472,460, filed May 22, 2003; and application No. 10/689,856, filed on October 20, 2003, which is a continuation-in-part of application No. 10/464,410, filed June 18, 2003, and is a continuation-in-part of application No. 10/464,834, filed June 18, 2003, both of which are continuation-in-part of application No. 10/400,293, filed March 26, 2003, now abandoned, and continuation-in-part of application No. 10/401,283, filed March 26, 2003, now abandoned, both of which claim the benefit of U.S. provisional application No. 60/450,237, filed February 25, 2003, and U.S. provisional application No. 60/420,383, filed October 21, 2002, each of which is incorporated herein by reference in its entirety.

Please delete the second full paragraph on page 7 of the application as filed, and replace it with the following paragraph:

Figure 3 illustrates exemplary fractions isolated or derived from hops. Figure 3A shows the alpha-acid genus (AA) and representative species humulone ($R = -CH_2CH(CH_3)_2$), cohumulone ($R = -CH(CH_3)_2$), and adhumulone ($R = -CH(CH_3)CH_2CH_3$); Figure 3B shows the isoalpha acid genus (IAA) and representative species isohumulone ($R = -CH_2CH(CH_3)_2$), isocohumulone ($R = -CH(CH_3)_2$), and isoadhumulone ($R = -CH(CH_3)CH_2CH_3$); Figure 3C shows the reduced isomerized isoalpha acid genus (RIAA) and representative species dihydro-isohumulone ($R = -CH_2CH(CH_3)_2$), dihydro-isocohumulone ($R = -CH(CH_3)_2$), and dihydro-isoadhumulone ($R = -CH(CH_3)CH_2CH_3$); Figure 3D shows the tetra-hydroisoalpha acid genus (THIAA) and representative species tetra-hydro-isohumulone ($R = -CH_2CH(CH_3)_2$), tetra-hydro-isocohumulone ($R = -$

CH(CH₃)₂), and tetra-hydro-isoadhumulone (R= -CH(CH₃)CH₂CH₃); Figure 3E shows and the hexa-hydroisoalpha acid (HHIAA) genus with representative species hexa-hydro-isohumulone (R= -CH₂CH(CH₃)₂) hexa-hydro-isocohumulone (R= -CH(CH₃)₂), and hexa-hydro-isoadhumulone (R= -CH(CH₃)CH₂CH₃).

Please delete the fifth full paragraph on page 14 of the application as filed, and replace it with the following paragraph:

As used herein, the term “reduced isoalpha acid” refers to alpha acids isolated from hops plant product and which subsequently have been isomerized and reduced, including cis and trans forms. Examples of reduced isoalpha acids (RIAA) include, but are not limited to, dihydro-isohumulone, dihydro-isocohumulone, and dihydro-isoadhumulone.

Please delete the sixth full paragraph on page 14 of the application as filed, and replace it with the following paragraph:

As used herein, the term “tetra-hydroisoalpha acid” refers to a certain class of reduced isoalpha acid. Examples of tetra-hydroisoalpha acid (THIAA) include, but are not limited to, tetra-hydro-isohumulone, tetra-hydro-isocohumulone and tetra-hydro-isoadhumulone.

Please delete the seventh full paragraph on page 14 of the application as filed, and replace it with the following paragraph:

As used herein, the term “hexa-hydroisoalpha acid” refers to a certain class of reduced isoalpha acid. Examples of hexa-hydroisoalpha acids (HHIAA) include, but are not limited to, hexa-hydro-isohumulone, hexa-hydro-isocohumulone and hexa-hydro-isoadhumulone.

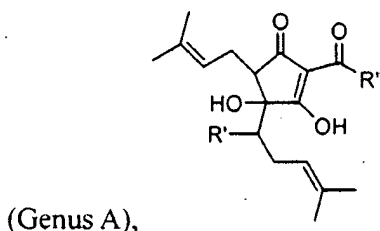
Please delete the second full paragraph on page 17 of the application as filed, and replace it with the following paragraph:

The invention provides compositions containing at least one fraction isolated or derived from hops (*Humulus lupulus*). Examples of fractions isolated or derived from hops are alpha acids, isoalpha acids, reduced isoalpha acids, tetra-hydroisoalpha acids,

hexa-hydroisoalpha acids, beta acids, and spent hops. Fractions isolated or derived from hops, include, but are not limited to, cohumulone, adhumulone, isohumulone, isocohumulone, isoadhumulone, dihydro-isohumulone, dihydro-isocohumulone, dihydro-isoadhumulone, tetrahydro-isohumulone, tetrahydro-isocohumulone, tetrahydro-isoadhumulone, hexahydro-isohumulone, hexahydro-isocohumulone, and hexahydro-isoadhumulone. Preferred compounds can also bear substituents, such as halogens, ethers, and esters.

Please delete the second paragraph on page 18 of the application as filed, and replace it with the following paragraph:

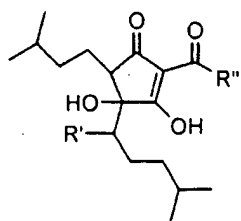
In another embodiment, compounds of the fractions isolated or derived from hops can be represented by a genus below:



wherein R' is selected from the group consisting of carbonyl, hydroxyl, OR, and OCOR, wherein R is alkyl; and wherein R'' is selected from the group consisting of CH(CH₃)₂, CH₂CH(CH₃)₂, and CH(CH₃)CH₂CH₃. Exemplary Genus A structures include isoalpha acids such as isohumulone, isocohumulone, isoadhumulone, and the like, and reduced isoalpha acids such as dihydro-isohumulone, dihydro-isocohumulone, dihydro-isoadhumulone, and ether or ester conjugates or halogenated modifications of the double bond.

Please delete the third paragraph on page 18 which bridges to page 19 of the application as filed, and replace it with the following paragraph:

In yet another embodiment, compounds of the fractions isolated or derived from hops can be represented by a genus below:



(Genus B),

wherein R' is selected from the group consisting of carbonyl, hydroxyl, OR, and OCOR, wherein R is alkyl; and wherein R'' is selected from the group consisting of $\text{CH}(\text{CH}_3)_2$, $\text{CH}_2\text{CH}(\text{CH}_3)_2$, and $\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$. Exemplary Genus B structures include tetra-hydroisoalpa acids such as tetra-hydro-isohumulone, tetra-hydro-isocohumulone and tetra-hydro-isoadhumulone, and the like, and hexa-hydroisoalpa acids such as hexa-hydro-isohumulone, hexa-hydro-isocohumulone and hexa-hydro-isoadhumulone, and ether or ester conjugates.

Please delete the second paragraph on page 19 of the application as filed, and replace it with the following paragraph:

As shown in Figure 3, examples of compounds of an ingredient isolated or derived from hops, include, but are not limited to, humulone, cohumulone, adhumulone, isohumulone, isocohumulone, isoadhumulone, dihydro-isohumulone, dihydro-isocohumulone, dihydro-isoadhumulone, tetrahydro-isohumulone, tetrahydro-isocohumulone, tetrahydro-isoadhumulone, hexahydro-isohumulone, hexahydro-isocohumulone, and hexahydro-isoadhumulone. The preferred compounds can bear substituents, as shown in the formula above.

Please delete the forth paragraph on page 19 of the application as filed, and replace it with the following paragraph:

The invention also provides compositions containing an analgesic and/or inflammatory compound or drug, for example, an NSAID, and a fraction or compounds isolated or derived from hops. For example, the invention provides compositions containing a fraction or compounds isolated or derived from hops, as disclosed herein, and one or more analgesic and/or inflammatory compounds or drugs such as NSAIDs. In a particular embodiment, the invention provides a composition comprising an isoalpa

acid or reduced isoalpha acid isolated from hops and a non-steroidal anti-inflammatory drug. The isoalpha acid can be selected from isohumulone, isocohumulone, and isoadhumulone. In another embodiment of the invention, the reduced isoalpha acid can be selected from dihydro-isohumulone, dihydro-isocohumulone, and dihydro-isoadhumulone.

Please delete the first paragraph on page 27 of the application as filed, and replace it with the following paragraph:

In an additional embodiment, the fraction isolated or derived from hops can be a compound selected from the group consisting of humulone, cohumulone, adhumulone, isohumulone, isocohumulone, isoadhumulone, dihydro-isohumulone, dihydro isocohumulone, dihydro-isoadhumulone, tetrahydro-isohumulone, tetrahydro-isocohumulone, tetrahydro-isoadhumulone, hexahydro-isohumulone, hexahydro-isocohumulone, and hexahydro-isoadhumulone. A composition of the invention can contain specific ranges of the active components, as disclosed herein.

Please delete the third paragraph on page 27 of the application as filed, and replace it with the following paragraph:

In another embodiment, the invention provides a composition comprising a reduced isoalpha acid isolated from hops and a non-steroidal anti-inflammatory compound. The reduced isoalpha acid can be, for example, dihydro-isohumulone, dihydro-isocohumulone, and dihydro-isoadhumulone.